## PATENT COOPERATIC . TREATY

	From the INTERNATIONAL BUREAU
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NOTIFICATION OF ELECTION  (PCT Rule 61.2)	Assistant Commissioner for Patents United States Patent and Trademark Office Box PCT Washington, D.C.20231 ETATS-UNIS D'AMERIQUE
Date of mailing (day/month/year) 12 September 2000 (12.09.00)	in its capacity as elected Office
International application No. PCT/US00/02026	Applicant's or agent's file reference 5452-PCT
International filing date (day/month/year) 26 January 2000 (26.01.00)	Priority date (day/month/year) 26 January 1999 (26.01.99)
Applicant SKIBO, Edward, B.	
1. The designated Office is hereby notified of its election made    X   in the demand filed with the International Preliminary 26 June 2000 (	Examining Authority on: 26.06.00) ational Bureau on:
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Form PCT/IB/331 (July 1992)

Facsimile No.: (41-22) 740.14.35

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#### WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



#### INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7:		(11) International Publication Number:	WO 00/43005
A61K 31/415	A1	(43) International Publication Date:	27 July 2000 (27.07.00)

(21) International Application Number:

PCT/US00/02026

(22) International Filing Date:

26 January 2000 (26.01.00)

(81) Designated States: CA, JP, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,

(30) Priority Data:

60/117,199

26 January 1999 (26.01.99)

US

Published

With international search report.

(71) Applicant (for all designated States except US): ARIZONA BOARD OF REGENTS, a body corporate of THE STATE OF ARIZONA, acting for and on behalf of ARIZONA STATE UNIVERSITY [US/US]; Tempe, AZ 85287 (US).

(72) Inventor; and

- (75) Inventor/Applicant (for US only): SKIBO, Edward, B. [US/US]; 5711 East Edgemont Drive, Scottsdale, AZ 85257 (US).
- (74) Agent: MYBECK, Richard, R.; Suite 10, 8010 East Morgan Trail, Scottsdale, AZ 85258 (US).

(54) Title: TREATMENT OF NEOPLASMS WITH THE YUJUNGAMYCINS

#### (57) Abstract

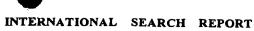
Pyrrolo[1,2- $\alpha$ ] benzimidazoles having structural formulae (A), (B) and (C) were prepared as reductive alkylating agents of DNA. In these compounds only the reduced (hydroquinone) form acts as the alkylating agent. DT-diaphorase is the prerequisite two-electron reducing enzyme which carries out the activation process. Depending on the cancer cell line organ and species source, the substrate and inhibition properties of the enzyme can vary widely. Therefore the design of the yujungamycins was to take advantage of subtle differences in the enzyme structure among cancer cell lines. In doing so, cancer- cell- selective drugs were designed possessing outstanding in vivo activity. The 3-substituent influences the reductive activation process and the substituents (amino, acetamido, and carbamido) were placed at this position with varying configuration (R and S). The variation in hydrogen bonding and stereochemistry permits the yujungamycins to recognize DT-diaphorase from select cancer cells resulting in a "magic bullet" directed toward such cells.

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International application No. PCT/US00/02026

A. CLASSIFICATION OF SUBJECT MATTER IPC(7) :A61K 31/415 US CL :514/394							
According to International Patent Classification (IPC) or to both national classification and IPC							
B. FIELDS SEARCHED							
Minimum documentation searched (classification system follows: 514/394	owed by classification symbols)						
Documentation searched other than minimum documentation to none	the extent that such documents are included in the fields searched						
Electronic data base consulted during the international search CAS ONLINE: yujungamycin or yujugamycin, ?aziridinyl	(name of data base and, where practicable, search terms used) ?, ?benzimidazol?, ?pyrrol? with cancer or neoplas?						
C. DOCUMENTS CONSIDERED TO BE RELEVANT							
Category* Citation of document, with indication, where	appropriate, of the relevant passages Relevant to claim No.						
A US 5,246,955 A (SKIBO et al) 21 S	eptember 1993. 1-10						
Further documents are listed in the continuation of Box  Special categories of cited documents:  'A* document defining the general state of the art which is not considered to be of particular relevance  'E* earlier document published on or after the international filing date  'document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)  'O* document referring to an oral disclosure, use, exhibition or other means	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone  "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is						
*P* document published prior to the international filing date but later than the priority date claimed	*&* document member of the same patent family						
Date of the actual completion of the international search 07 MARCH 2000	Date of mailing of the international search report  0.6 APR 2000						
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer  KIMBERLY JORDAN  Telephone No. (703) 308-1235						

#### PATENT COOPERATION TREATY

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## **PCT**

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#### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

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Applicant's or agent's file reference 5452-PCT	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)			
International application No.	International filing date (day/n	nonth/year) Priority date (day/month/year)			
PCT/US00/02026	26 JANUARY 2000	26 JANUARY 1999			
International Patent Classification (IPC) of IPC(7): A61K 31/415 and US Cl.: 514	or national classification and IPC 4/394	c .			
Applicant ARIZONA BOARD OF REGENTS, A BEHALF OF ARIZONA STATE UNIV	BODY CORPORATE OF TH	IE STATE OF ARIZONA, ACTING FOR AND ON			
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3. This report contains indication	s relating to the following it	ems:			
3. This report contains indications relating to the following items:  I X Basis of the report  II Priority  III Non-establishment of report with regard to novelty, inventive step or industrial applicability  IV Lack of unity of invention  V X Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement  VI Certain documents cited  VII Certain defects in the international application  VIII Certain observations on the international application					
Date of submission of the demand	Date	of completion of this report			
26 JUNE 2000		B AUGUST 2000			
Name and mailing address of the IPEA/U  Commissioner of Patents and Tradema Box PCT  Washington, D.C. 20231  Facsimile No. (703) 305-3230	urks R	injed officer    Within   nurrence for  those No. (703) 308-1235			



# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.	
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#### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/02026

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement					
l. statement					
Novelty (N)	Claims	1-10	YES		
	Claims	none	NO		
Inventive Step (IS)	Claims	1-10	YES		
	Claims	none	NO		
Industrial Applicability (IA)	Claims	1-10	_ YES		
	Claims	none	_ NO		
Claims 1-10 meet the criteria set out in PCT compositions or methods of treating neoplast in the oncology field.	ic diseases with	), because the prior art does not teach or fairly suggest yujungamycins. The methods and compositions would b	e useful		
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